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15 DIFFUSE AIR-SPACE OPACITIES

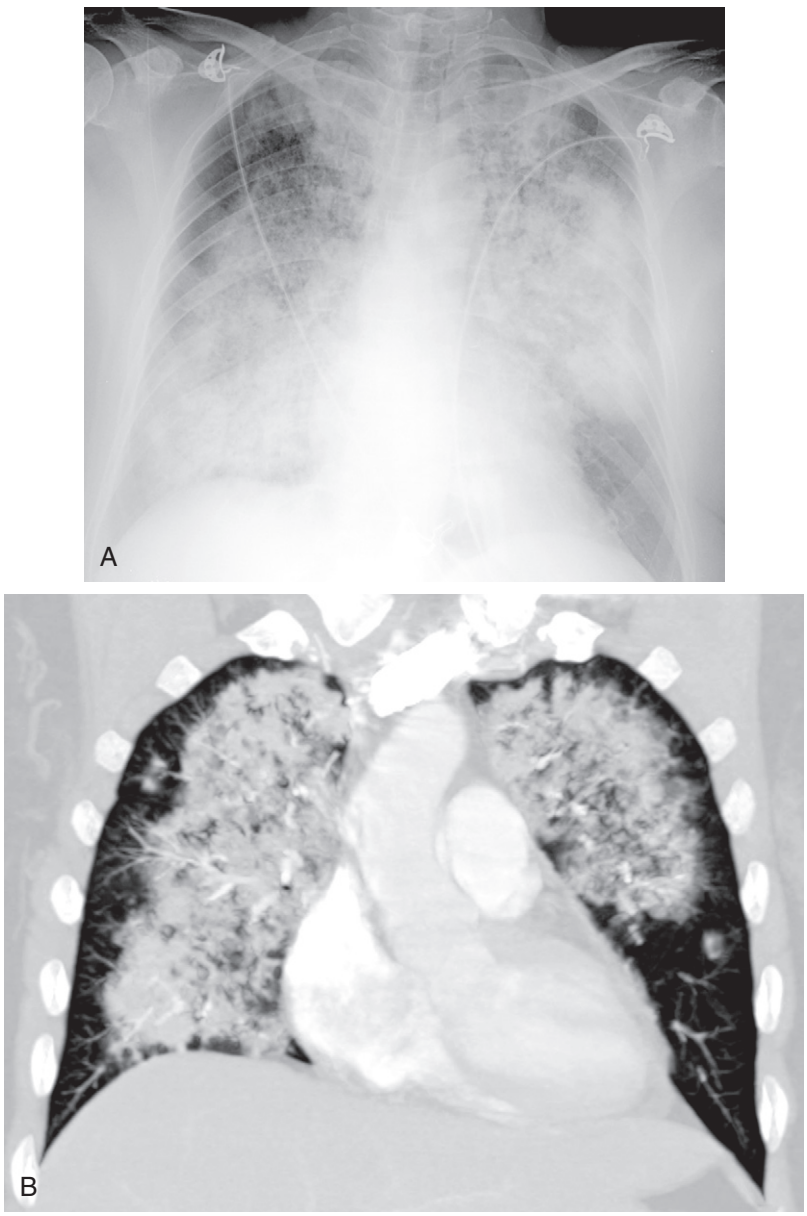

Figure 15-1

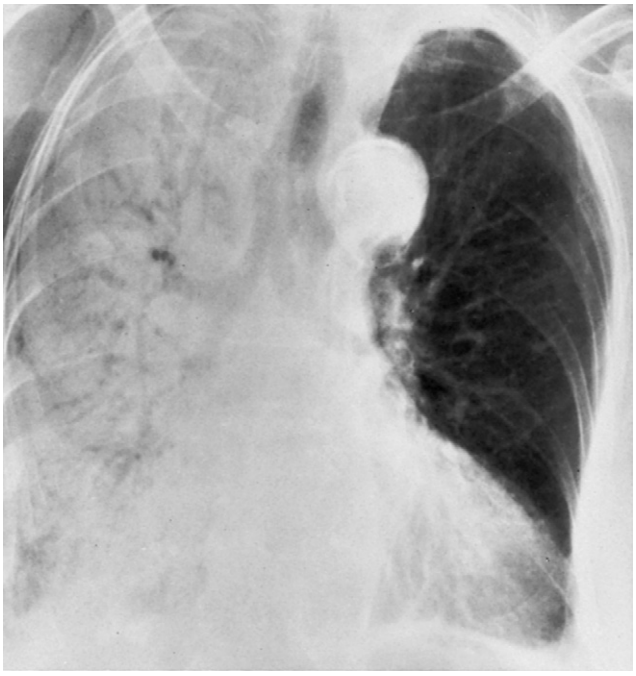

Figure 15-2

QUESTIONS

1. Examine Figures 15-1, *A* and *B*. Which of the following are signs of air-space disease?
   a. Diffuse coalescent opacities.
   b. Air bronchograms.
   c. Acinar rosettes.
   d. Fine reticular opacities.
   e. Air alveolograms.

2. The asymmetric distribution of the diffuse coalescent opacities in Figure 15-2 is suggestive of which diagnosis?
   a. Bronchopneumonia.
   b. Goodpasture's syndrome.
   c. Chronic renal failure.
   d. Alveolar proteinosis.
   e. Congestive heart failure.

3. A 24- to 48-hour delay in the development of pulmonary edema is commonly observed in which of the following conditions?
   a. Congestive heart failure.
   b. Pulmonary emboli.
   c. Smoke inhalation.
   d. Heroin reaction.
   e. High-altitude pulmonary edema.

Chart 15-1 DIFFUSE AIR-SPACE OPACITIES

I. Edema
  A. Cardiac failure
  B. Noncardiac (see Chart 15-2)
II. Exudate (pneumonias)
  A. Bacteria[69,70,154]
  B. Viruses[125,314,495]
  C. Mycoplasma[205,338]
  D. Fungi[63,123,482,580,679]
  E. *Pneumocystis jiroveci* pneumonia (also known as PCP)[84,96,126,151]
  F. Parasites (Strongyloidiasis)[810]
  G. Aspiration
  H. *Rickettsiae* (Rocky Mountain spotted fever)[437,475]
  I. Tuberculosis[527]
  J. Severe acute respiratory syndrome (SARS)[60,97,530,534]
III. Hemorrhage
  A. Anticoagulation therapy
  B. Bleeding diathesis (e.g., leukemia)
  C. Disseminated intravascular coagulation (18- to 72-hour delay)[576]
  D. Blunt trauma[764] (pulmonary contusion, usually is not diffuse)
  E. Vasculitis
    1. Infections (mucormycosis, aspergillosis, Rocky Mountain spotted fever)
    2. Wegener's granulomatosis[427,467,569,761] (classic and variant forms)
    3. Goodpasture's syndrome[324,569]
    4. Systemic lupus erythematosus[569]
  F. Idiopathic pulmonary hemosiderosis[211,742]
  G. Infectious mononucleosis[749]
IV. Tumor
  A. Bronchioloalveolar-cell carcinoma[57,503]
  B. Lymphoma and rare lymphocytic disorders including:
    1. Lymphocytic interstitial pneumonitis[68]
    2. Angioblastic lymphadenopathy[386]
    3. Mycosis fungoides[354]
    4. Waldenström's macroglobulinemia
V. Other
  A. Pulmonary alveolar proteinosis[226,337,589,623]
  B. Adult respiratory distress syndrome (ARDS)[171,368,369,384,546,822]
  C. Acute interstitial pneumonia (AIP)[11,347]
  D. Sarcoidosis (very unusual)[500,589,599]
  E. Desquamative interstitial pneumonitis (DIP)
  F. Mineral oil aspiration (exogenous cholesterol pneumonia)
  G. Eosinophilic lung disease[113,234,365]
  H. Chemical pneumonitis from intravenous hydrocarbon
  I. Respiratory distress syndrome of the newborn[589,726]
  J. Drug reactions (see Chart 15-3)

Chart 15-2 NONCARDIAC PULMONARY EDEMA

I. Chronic renal failure
II. Toxic inhalations
  A. Nitrogen dioxide (silo-filler's disease)
  B. Sulfur dioxide[101]
  C. Smoke[377,575]
  D. Beryllium
  E. Cadmium
  F. Silica (very fine particles) (silico-proteinosis)[393]
  G. Dinitrogen tetroxide[150]
  H. Carbon monoxide[696]
III. Anaphylaxis (penicillin, transfusion,[87] radiologic contrast medium[276])
IV. Narcotics (morphine, methadone, cocaine, heroin)[605,635,831]
V. Drug reaction (e.g., interleukin-2 therapy,[120,656] β-adrenergic drugs[507])
VI. Acute airway obstruction[547] (e.g., foreign body)
VII. Near-drowning[577]
VIII. High altitude[344]
IX. Fluid overload
X. Cerebral (trauma, stroke, tumor)[599]
XI. Hypoproteinemia
XII. Pulmonary embolism
XIII. ARDS (early stages)[167,368,384]
XIV. Pancreatitis[631]
XV. Amniotic fluid embolism[682]
XVI. Fat embolism
XVII. Reexpansion following treatment of pneumothorax
XVIII. Organophosphate insecticide ingestion[445]
XIX. Hanta virus pulmonary syndrome[384]

Chart 15-3 PULMONARY DRUG REACTIONS

I. Edema
  A. Narcotics[635,831]
  B. Radiologic contrast[276]
  C. Interleukin-2 therapy[120,656]
  D. β-adrenergic drugs[507]
II. Hemorrhage[626]
  A. Anticoagulants
  B. Amphotericin B
  C. Cytarabine
  D. Cyclophosphamide
  E. Penicillamine
III. Diffuse alveolar damage (DAD)[626]
  A. Bleomycin
  B. Busulfan
  C. Carmustine
  D. Cyclophosphamide
  E. Gold
  F. Melphalan
  G. Mitomycin

Continued

Chart 15-3 PULMONARY DRUG REACTIONS—cont'd

IV. Eosinophilic Pneumonia[626]
- A. Nitrofurantoin
- B. Nonsteroidal antiinflammatory drugs
- C. Paraaminosalicylic acid
- D. Penicillamine
- E. Sulfasalazine

V. Cryptogenic organizing pneumonia (COP)[626]
- A. Amiodorone[551]
- B. Bleomycin
- C. Cyclophosphamide
- D. Gold
- E. Methotrexate
- F. Nitrofurantoin
- G. Penicillamine
- H. Sulfasalazine

VI. Nonspecific interstitial pneumonitis (NSIP)[626]
- A. Amiodarone
- B. Carmustine
- C. Chlorambucil
- D. Methotrexate

Modified from Rossi SE, Erasmus JJ, McAdams HP, et al. Pulmonary drug toxicity: radiologic and pathologic manifestations. *Radiographics.* 2000;20:1245-1259. Used with permission.

Discussion

The classic radiologic appearance of diffuse air-space consolidation[24] is shown in Figures 15-1, *A* and *B*, and consists of diffuse coalescent or confluent opacities with ill-defined borders; a butterfly-shaped perihilar distribution; ill-defined nodular opacities around the periphery of the process ("acinar pattern")[754,826]; and interspersed, small lucencies.[589,592] Air-filled bronchi surrounded by the confluent opacities are seen as dark, branching shadows. These were described by Fleischner[210] as the "visible bronchial tree" and are commonly referred to as *air bronchograms*[197] (see Fig 15-2). The small, interspersed lucencies represent groups of air-filled alveoli surrounded by airless, consolidated lung. The term *air alveologram* was applied to these lucencies by Felson[197]; they are the alveolar equivalent of the air bronchogram. Other features of air-space consolidation include the lobar or segmental distribution of opacities (see Chapter 14) and a tendency for the process to be labile, that is, changing in severity over a short period of time. Observation of the changing character of the opacities requires serial roentgenograms. (The only incorrect answer to question 1 is *d*.) Diffuse ground-glass opacity is occasionally used to describe less-opaque, diffuse confluent patterns seen on plain film and is more commonly used in reporting high-resolution computed tomography (HRCT). This differs from consolidation in degree of opacity and implies minimal disease. Ground-glass opacities appear on HRCT as gray areas of confluent attenuation that fail to obliterate normal vascular shadows. Ground-glass opacity demonstrated by HRCT results from minimal filling of the alveolar spaces or from thickening of the alveolar walls and septal interstitium.[174]

PULMONARY EDEMA

Cardiac Pulmonary Edema

Pulmonary alveolar edema is a classic example of a diffuse air-space–filling process (Chart 15-1). The presence of alveolar edema, however, does not imply the absence of interstitial edema. For example, cardiac pulmonary alveolar edema is always preceded by interstitial edema, but the extensive alveolar consolidation may obscure the fine, reticular pattern of the interstitial process. This is in effect a microscopic version of Felson's silhouette sign,[197] because the material in the alveolar space has the same opacity as the edema fluid in the interlobular septa and bronchovascular bundles. Radiologic documentation of the underlying interstitial process entails examination of areas not significantly involved by the alveolar-filling process. When alveolar pulmonary edema is secondary to congestive heart failure, the alveolar edema often has a perihilar distribution, and Kerley's B lines may be present in the costophrenic angles. The latter sign indicates an underlying interstitial process. Other radiologic signs that may be associated with cardiopulmonary edema and can be helpful in suggesting the diagnosis include: (1) prominence of the upper-lobe vessels;[586] (2) indistinctness of vessels;[384] (3) peribronchial cuffing;[506] (4) increased width of the vascular pedicle;[506] (5) pleural effusion, frequently with fluid in the fissures (see Fig 4-3); and (6) cardiac enlargement with a left ventricular prominence. Correlation of such findings with clinical findings usually confirms the diagnosis. An electrocardiogram indicating cardiac enlargement or an old or acute myocardial infarction is also supportive evidence, whereas an S-3 heart sound, neck vein distention, hepatomegaly, or peripheral edema usually confirm the diagnosis of congestive failure. Also, ausculation over the lungs usually reveals characteristic basilar rales.

Occasionally, the alveolar edema is not distributed uniformly. As a result of gravity, the edema fluid has a predominantly lower lobe distribution when the patient is upright, but when the patient is supine, the fluid tends to have a more posterior distribution. When the patient favors one side, the fluid tends to gravitate to the dependent side. Other causes for atypical or nonuniform distribution of pulmonary edema are usually of pulmonary origin. The best known of these is severe emphysema, which results in patchy distribution of the alveolar edema. Presumably, loss of vasculature in the emphysematous areas of the lung results in the development of edema in the more normal areas (Fig 15-3). Pulmonary embolism is another complication of pulmonary edema that may result in a nonuniform or patchy distribution of the alveolar edema. Two factors may determine the distribution of the air-space edema following pulmonary embolism: (1) Abrupt interruption of perfusion to an area of lung may prevent the development of typical pulmonary edema. For example, large emboli may occlude the lower-lobe vessels so completely that the entire pulmonary blood flow is diverted to the upper lobes. The radiologic result is hyperlucency of the lower lobe and edema in the upper lobe. (2) Ischemia may influence the radiologic appearance of pulmonary edema complicated by pulmonary embolism. Severe ischemia of the lung can give rise to hemorrhagic pulmonary edema, and because pulmonary emboli tend to be scattered, this can lead to the appearance of multifocal ill-defined opacities (see Chapter 16). The significance of this pattern is difficult to determine because the normal resolution of pulmonary edema is often not uniform, thus clinical correlation is essential. When the plain film reveals patchy air-space consolidation, lung scanning is frequently not diagnostic, and definitive diagnosis of pulmonary embolism is made by pulmonary angiography[699] or computed tomography (CT) angiography.

Concomitant infection is another cause of uneven distribution of pulmonary edema. Like the diagnosis of pulmonary embolism, this requires correlation with the clinical history. An elevated temperature, leukocytosis, or purulent sputum should prompt a bacteriologic study to rule out superimposed pneumonia.

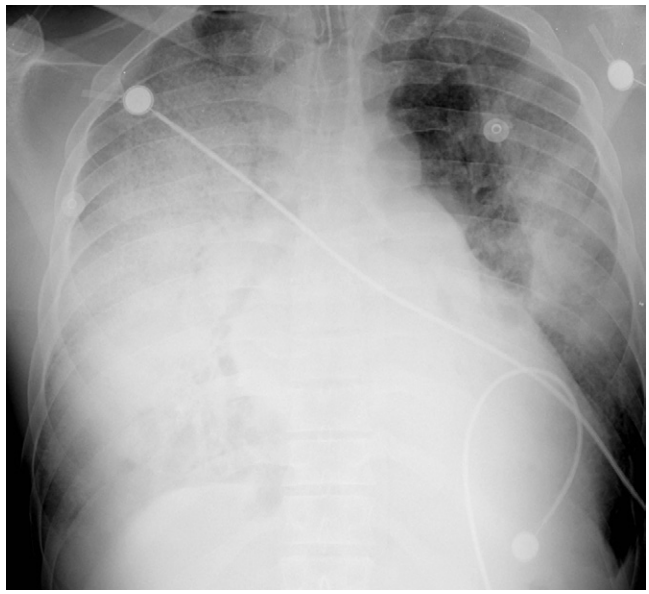

Figure 15-3 Pulmonary edema is a common cause of diffuse confluent opacities. The distribution may be asymmetric from a number of cuases. In this case, left-upper lobe, bullous emphysema is the cause of sparing of the medial, left upper lobe.

Cardiac enlargement in combination with diffuse alveolar opacities that are otherwise characteristic of pulmonary edema is not always a reliable indicator that the patient's primary problem is a cardiac disorder. For instance, chronic renal failure with uremia can cause pulmonary edema (uremic pneumonitis) as well as hypertension and associated heart disease, with the result of cardiac enlargement. Not only does uremia cause true cardiomegaly, which is probably related to chronic hypertension, but it also may cause pericardial effusion. Thus, the pulmonary edema that results from chronic renal failure and uremia is typically associated with enlargement of the cardiac silhouette. Correlation with the clinical history should readily identify uremic pneumonitis.

In contrast to pulmonary alveolar edema and cardiac enlargement, the presence of a normal-sized heart might suggest a noncardiac form of pulmonary edema, but there are situations in which such patients may actually have cardiac pulmonary edema. These include acute cardiac arrhythmias and acute myocardial infarction, which result in pulmonary edema before dilation of the heart. Thus, there are at least two mechanisms for cardiac pulmonary edema with a normal-sized heart.

Noncardiac Pulmonary Edema

The preceding discussion suggests that the radiologic appearance of noncardiac pulmonary edema is similar to that of cardiac pulmonary edema.[693] In general, the most helpful radiologic feature for distinguishing the two is the presence or absence of cardiac enlargement. Accurate assessment of heart size is often difficult. Technical factors—including supine and anteroposterior positioning, especially when done with portable units—may all contribute to cardiac magnification. Patient condition may also lead to inaccurate cardiac size estimation. Patients with emphysema often have cardiac enlargement, although the plain film is suggestive of a normal or even small heart size. Aggressive intravenous (IV) fluid resuscitation may actually enlarge the heart and cause pulmonary edema. The evaluation of serial films is especially useful for distinguishing a number of the causes of noncardiac edema, because the evolution of the edema may be strikingly different. Many of the entities listed in Chart 15-2 may result in acute alveolar edema in the absence of the pulmonary vascular and

interstitial changes that precede the edema, owing to either renal failure or cardiac failure. These entities tend to occur in very acute cases of pulmonary edema and are often best diagnosed by clinical correlation,[5] as is shown in the following discussions of acute toxic inhalations, near drowning, acute airway obstruction, drug reactions, and ARDS.

Acute Toxic Inhalations

Nitrogen dioxide inhalation (silo-filler's disease) is an excellent model for acute toxic pulmonary edema. In the first few days after a grain storage silo is filled, nitrogen dioxide forms. The gas reacts with water in the respiratory tract to produce an irritation of the tracheobronchial tree and alveoli. In the acute phase, this disease has the radiologic appearance of bilateral diffuse alveolar edema. This phase is usually followed within a few days or weeks by complete resolution, although bronchiolitis obliterans may develop weeks to months later as a result of the small airway injury. Roentgenograms from patients with bronchiolitis obliterans often show a fine nodular or reticular pattern. The other chemicals listed in Chart 15-2 produce a similar reaction.

Smoke is a common cause of acute toxic inhalation. Because the most common radiologic presentation of toxic smoke inhalation is a normal chest film, chest roentgenography is not a reliable technique for assessing the acute effects of smoke inhalation. The radiologic appearance of pulmonary edema may be delayed by as much as 24 to 48 hours (answer to question 3 is *c*). Putman et al.[575] suggest that arterial hypoxemia is a more sensitive index of pulmonary injury from smoke inhalation. Another important method for evaluating smoke inhalation is to determine the amount of carboxyhemoglobin in the blood. Levels above the normal mean of 2.01% in nonsmokers and 7.22% in smokers reflect carbon monoxide poisoning with potential concomitant lung damage.

Near Drowning

Near drowning[577] is another important cause of noncardiac pulmonary edema (Fig 15-4). The history should confirm the diagnosis; however, aspiration of water provides

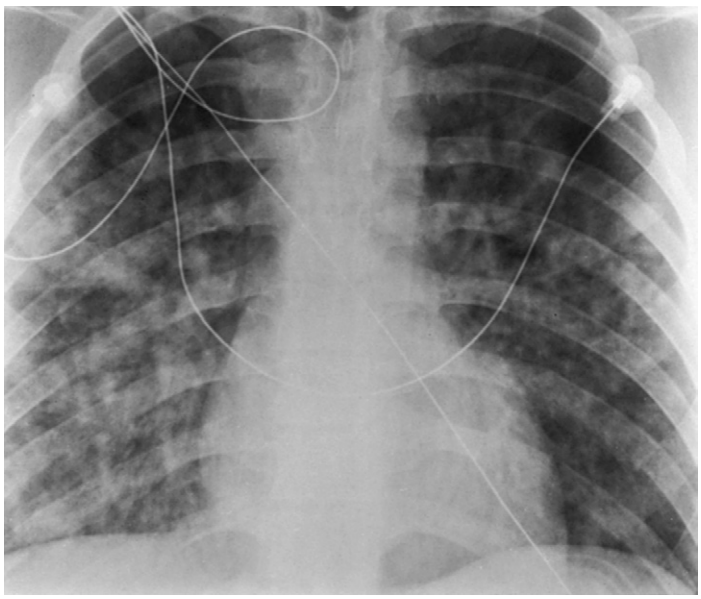

Figure 15-4 Near drowning produces diffuse bilateral air-space consolidations with a normal heart size. The history is essential to confirm the diagnosis. The radiologic appearance is indistinguishable from that of the other causes of noncardiac pulmonary edema.

only a partial explanation for the diffuse alveolar opacities that may develop in near-drowning victims. Again, there may be a delay of 24 to 48 hours before edema develops. Other mechanisms that may contribute to the development of this type of edema include prolonged hypoxia, respiratory obstruction, and fibrin degradation. Fibrin degradation raises the possibility of a subclinical, consumptive coagulopathy with microembolization, which may lead to a diffuse pulmonary capillary leak and thus to pulmonary edema. Severe hypoxia may occur in a near-fatal–drowning victim even when the initial chest roentgenogram is normal. Patients should therefore be followed for 24 to 48 hours to exclude a significant pulmonary injury.

Acute Airway Obstruction

The diagnosis of acute airway obstruction is usually made on the basis of the clinical history. The obstruction is frequently an aspirated object, such as a large bolus of food or a surgical sponge. The resultant pulmonary edema is usually related to severe hypoxia. This mechanism may be nearly identical to that described for near drowning. The collection of alveolar fluid is most likely due to a diffuse alveolar leak caused by severe injury to the alveolar capillary membrane.[547]

Drug Reactions

Adverse reactions to a variety of drugs (Chart 15-3) may cause both acute and chronic pulmonary responses.[20,73] These reactions have been described as chemotherapy lung,[698] but a large variety of drugs have pulmonary complications. These include antibiotics, narcotics, heart medications, arthritis drugs, and a number of the chemotheraputics. The acute drug reactions may cause rapid development of diffuse confluent air-space opacities or patchy, multifocal confluent opacities (as seen in Chapter 16). These acute reactions are the result of edema, hemorrhage, or DAD that may resemble ARDS. Subacute and chronic reactions include eosinophilic pneumonia, COP, and NSIP. The more chronic reactions cause air-space opacities in the early stages but may later progress to cause reticular opacities indicating a fibrotic reaction. Pleural effusions (see Chart 4-1) may also be associated with some of these reactions. This is especially true of drugs that are known to cause a lupus-like reaction.[625]

Edema is an acute response to substances that cause anaphylaxis and may be seen in patients with allergic reactions to IV radiologic contrast. Acute alveolar edema may also occur following administration of morphine, heroin, and other opiates. Cocaine is reported as a cause of both cardiac and noncardiac pulmonary edema.[267,605] Although the mechanism for the noncardiac pulmonary edema is unknown, it is generally believed to represent an idiosyncratic reaction with an alveolar capillary injury. Since the opiates cause central nervous system depression, there may also be a relationship to neurogenic edema. Methadone, a slow-acting narcotic, may cause a slower onset of edema than heroin or morphine, and may also resolve more slowly.[267,831] The typical plain film pattern for narcotic-induced edema is diffuse, bilateral, confluent air-space opacification without cardiomegally and without pleural effusion. In contrast with the narcotics, the allergic edema of interlukin-2 commonly causes interstitial edema (as seen in Chapter 18) with septal lines and peribronchial edema.[120,384,656] This so-called allergic edema infrequently becomes more severe with the development of alveolar edema.[384]

Drug reactions that result in pulmonary hemorrhage produce radiologic appearances that are identical to those of alveolar edema. The plain film may show either diffuse, symmetrical, confluent opacities with a perihilar or basal distribution or the pattern of multifocal opacities. Sometimes HRCT may show that the distribution is more patchy or multifocal than suspected from the plain film. Additional HRCT findings include ground-glass opacities that indicate less severe alveolar hemorrhage.

Anticoagulants, amphotericin B, and some of the cytotoxic drugs are all possible causes of acute pulmonary hemorrhage.[626]

Acute DAD causes permeability edema with the radiologic appearance of diffuse confluent opacities that may sometimes appear multifocal. Therefore, in its early stages, DAD may be indistinguishable from hydrostatic pulmonary edema. The acute edema is rapidly followed by cellular necrosis, inflammation, and later fibrosis. Therefore, drug reactions are another cause of ARDS. Bleomycin, busulfan, and cyclophosphamide are all possible causes of DAD.

Eosinophilic pneumonia is a true allergic reaction. Diffuse confluent air-space opacities with a peripheral distribution are typical. Histologic changes include infiltration of alveolar walls with eosinophils and other inflammatory cells. Peripheral eosinophilia is also a common finding. Eosinophilic pneumonia responds well to withdrawal of the medication, but sometimes requires steroid therapy for complete resolution. Nitrofurantoin is a urinary antibiotic that may cause eosinophilic pneumonia.

COP, previously known as BOOP (bronchiolitis obliterans organizing pneumonia), is more likely to produce multiple areas of diffuse, confluent opacity. Like eosinophilic pneumonia, the opacities tend to be in the periphery of the lung. CT often shows the areas of consolidation to be more nodular than expected from the plain film. Even though there is histologic evidence of fibrosis, this reaction usually responds well to withdrawal of the drug and steroid therapy.[626] Amiodorone, bleomycin, methotrexate, and nitrofurantoin are all possible causes of COP.

NSIP is more likely to present with patchy or multifocal basilar opacities that may appear confluent on the plain film. HRCT often shows mainly ground glass with some reticular opacities. This reaction is more likely to progress to interstitial fibrosis with reticular opacities, honeycombing, and traction bronchiectasis.[626] Amiodarone and methotrexate are also causes of NSIP.

The diagnosis of drug reaction is best suggested by a history of medication with any of the drugs known to produce pulmonary reactions.[625] In patients who are undergoing chemotherapy for cancer, the differential includes: (1) opportunistic infection, (2) diffuse hemorrhage, (3) drug reaction, and (4) spread of the primary tumor.[124]

Adult Respiratory Distress Syndrome

ARDS is a complex clinical syndrome that may occur after a variety of severe pulmonary injuries,[171] including trauma, shock, sepsis, severe pulmonary infection, transfusion reaction, or cardiopulmonary bypass. These conditions cause an alveolar-capillary injury with leakage of edema fluid into the alveolar spaces. This is so severe that increasing concentrations of inspired oxygen are required to maintain adequate arterial oxygen saturation, while at the same time high ventilator pressures are needed to combat the decreasing lung compliance. The radiologic appearance is that of diffuse, coalescent opacities similar to those described for alveolar edema, alveolar hemorrhage, or diffuse air-space pneumonia. The sequence of events in patients with ARDS, however, is different from that in patients with typical pulmonary edema. Unlike cardiac pulmonary edema, which clears in response to therapy, the edema in ARDS may persist for days to weeks. As the diffuse coalescent opacities begin to clear, an underlying reticular pattern emerges. Patients who succumb to the illness usually have a complex pulmonary reaction that includes the formation of hyaline membranes, extensive fibrosis, and the development of areas of organizing pneumonia. Grossly, the lungs are stiff and firm. The mechanisms for this catastrophic course are not completely understood. It has been suggested that diffuse intravascular clotting and platelet aggregation within the capillary bed (disseminated intravascular coagulation) probably lead to interstitial edema, altered capillary permeability, atelectasis, and hyaline-membrane formation. This is pathologically described as DAD and includes injury to the capillary endothelium and alveolar epithelium.[384] Oxygen toxicity may

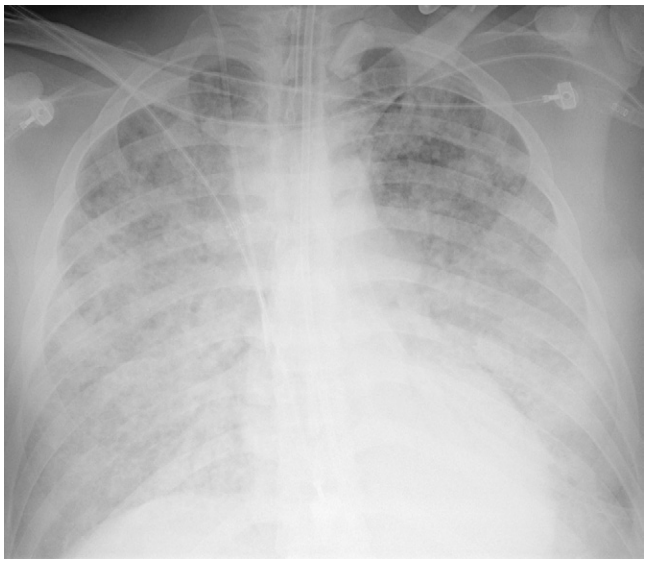

Figure 15-5 Diffuse pulmonary consolidations with air bronchograms in this case are the result of ARDS. This appearance is radiologically indistinguishable from diffuse pneumonia and other causes of pulmonary alveolar edema. In the early stages of DAD, the alveoli are filled by edema resulting from alveolar-capillary leak.

also be a factor in the pathogenesis of many cases of ARDS. In addition, bacterial superinfection is very common. This entity should be suspected on the basis of the clinical presentation and the presence of persistent, diffuse coalescent opacities (Fig 15-5).

Reexpansion pulmonary edema is an infrequent complication of pneumothorax. This is probably the consequence of alveolar capillary injury initiated by ischemia. It develops following the treatment of a large pneumothorax with near-complete collapse of the lung. The history often suggests a delay in treatment of more than 24 hours (Figs 15-6, *A* and *B*).

Acute Interstitial Pneumonia

AIP is a fulminant form of interstitial pneumonia that was originally described by Hamman and Rich.[292] Because it is an idiopathic interstitial pneumonia, AIP is often grouped with usual interstitial pneumonia, desquamative interstitial pneumonia, and NSIP. It has a different clinical course in that it occurs in previously healthy individuals and is rapidly progressive with a poor prognosis. The histologic findings are described as DAD and are similar to findings of ARDS. It has even been described as an idiopathic form of ARDS. The first phase is an exudative reaction that is followed by a proliferative reaction. The plain film findings typically show diffuse air-space opacities. HRCT may show additional findings of ground-glass opacities and reticular or linear opacities. The proliferative phase may begin after the first week. Additional CT findings that result from the retracting fibrosis during the proliferative phase may include architectural distortion, traction bronchiectasis, and cystic spaces.[11,347]

Other

Other causes of pulmonary edema that must be diagnosed on the basis of the clinical history include high-altitude pulmonary edema,[344] amniotic fluid embolism,[682] and fat embolism. As indicated in the discussion of smoke inhalation and near drowning, there may be a delay in the development of the diffuse, coalescing opacities with fat

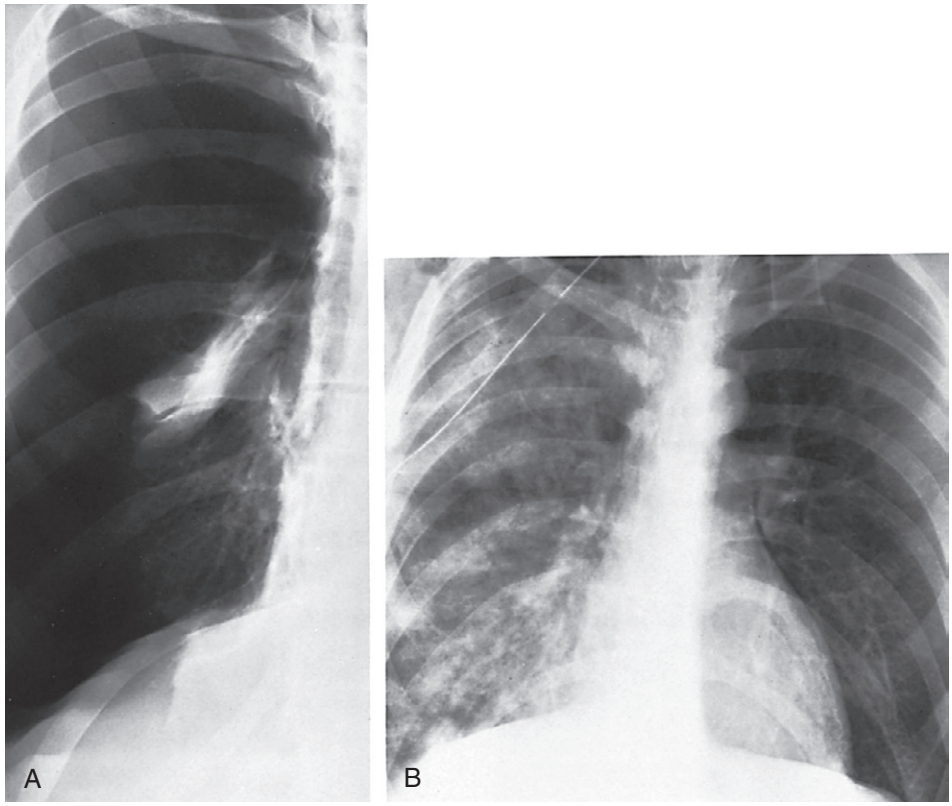

Figure 15-6 **A,** This large right pneumothorax has caused near-complete collapse of the right lung. **B,** Following treatment of the pneumothorax with a thoracostomy tube, the patient developed diffuse confluent opacity throughout the right lung. This has been described as reexpansion pulmonary edema.

embolism, but it should not exceed the time of the fracture by more than 24 to 48 hours. Repositioning or orthopedic manipulation of a fracture occasionally accounts for fat emboli occurring days to weeks after the initial fracture. In the absence of a history of manipulation, however, the development of pulmonary opacities from days to weeks after a fracture is more suggestive of other diagnoses, such as venous thromboembolism or pneumonia.

Pulmonary Hemorrhage

Hemorrhage is an important cause of diffuse coalescent opacities because it may lead to extensive air-space consolidation (see Figs 15-1, *A* and *B*). Some of the causes of pulmonary hemorrhage, such as anticoagulant therapy and pulmonary contusion, are easily identified from the clinical history. Hemoptysis is a common clinical finding because a large amount of blood fills the lungs.

Some of the bleeding disorders that may lead to pulmonary hemorrhage are hemophilia, anticoagulation therapy, and hematologic malignancy. The differential or diffuse alveolar consolidation in the leukemic patient is that of: (1) opportunistic infection, (2) drug reaction, (3) diffuse hemorrhage, (4) leukemic infiltration, and (5) pulmonary edema. Severe hemoptysis confirms the diagnosis of diffuse pulmonary hemorrhage in such a clinical setting, but the absence of hemoptysis does not exclude the diagnosis.

Trauma is not a common cause of diffuse pulmonary hemorrhage, but in the setting of severe trauma, diffuse air-space opacities may result from pulmonary contusion

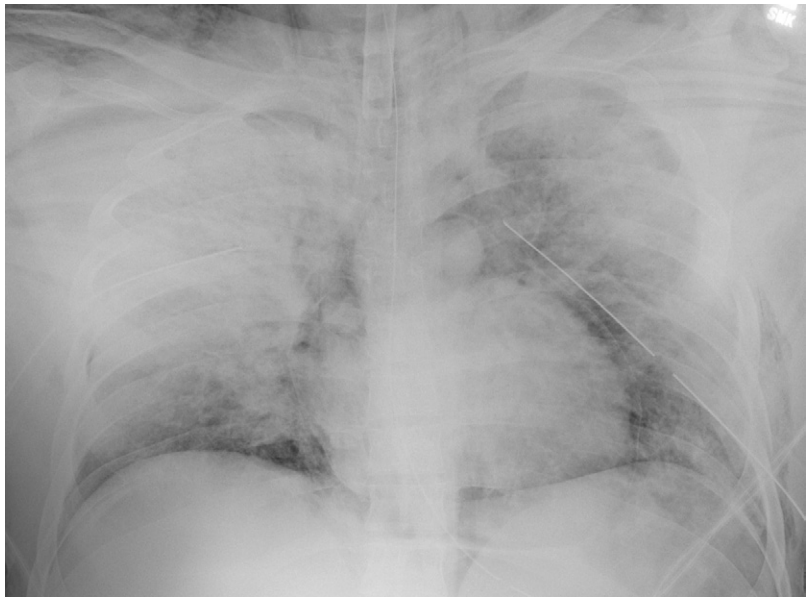

Figure 15-7 Pulmonary contusion should be suspected as the cause of diffuse air-space opacites in patients who have sustained major thoracic trauma. In this case, the additional finding of lucency around the heart is the result of a traumatic pneumopericardium.

(Fig 15-7). More frequently, trauma results in asymmetric, localized, or multifocal areas of contusion (Figs 15-8, *A* and *B*). Often there are associated fractures and pleural effusion. The history confirms the diagnosis.

Goodpasture's syndrome,[665] although not a common entity, must be seriously considered in a patient with hemoptysis, hematuria, and diffuse air-space consolidations. The diagnosis is usually confirmed by renal biopsy with specific, immunofluorescent stains. Because these patients have antibodies to their glomerular basement membrane, the condition has been renamed *antiglomerular basement membrane disease*.[569]

Idiopathic pulmonary hemosiderosis is another rare pulmonary disease that causes diffuse pulmonary hemorrhage. The radiologic pattern depends on the stage of the disease. In the acute phases, there are bilateral, diffuse coalescent opacities with air bronchograms. As the disease resolves, the clearing may be patchy, leaving the multifocal ill-defined opacities described in Chapter 16. This entity tends to be recurrent with the development of an interstitial pattern that is frequently of a fine, reticular nature and occurs as a late complication of the disease. This generally follows many recurrences of the acute alveolar hemorrhage. During the phases of the hemorrhage, the fine, reticular pattern is obscured by extensive alveolar consolidation.

Wegener's granulomatosis is a diffuse pulmonary vasculitis that may produce either localized or diffuse pulmonary hemorrhage (see Figs 15-1, *A* and *B*). This diagnosis is easily confirmed when the classic Wegener's triad of pulmonary, nasopharyngeal, and renal involvement is present. The limited form of Wegener's granulomatosis requires lung biopsy for confirmation. Other patterns associated with this entity include multiple ill-defined opacities and multiple lesions that may cavitate (see Chapters 16 and 24). Systemic lupus erythemetosus is another collagen vascular disease that sometimes causes diffuse pulmonary hemorrhage.[569]

INFLAMMATION

Acute pulmonary infections are a major consideration in the differential of diffuse coalescent opacities. The entity is commonly distinguished from pulmonary edema

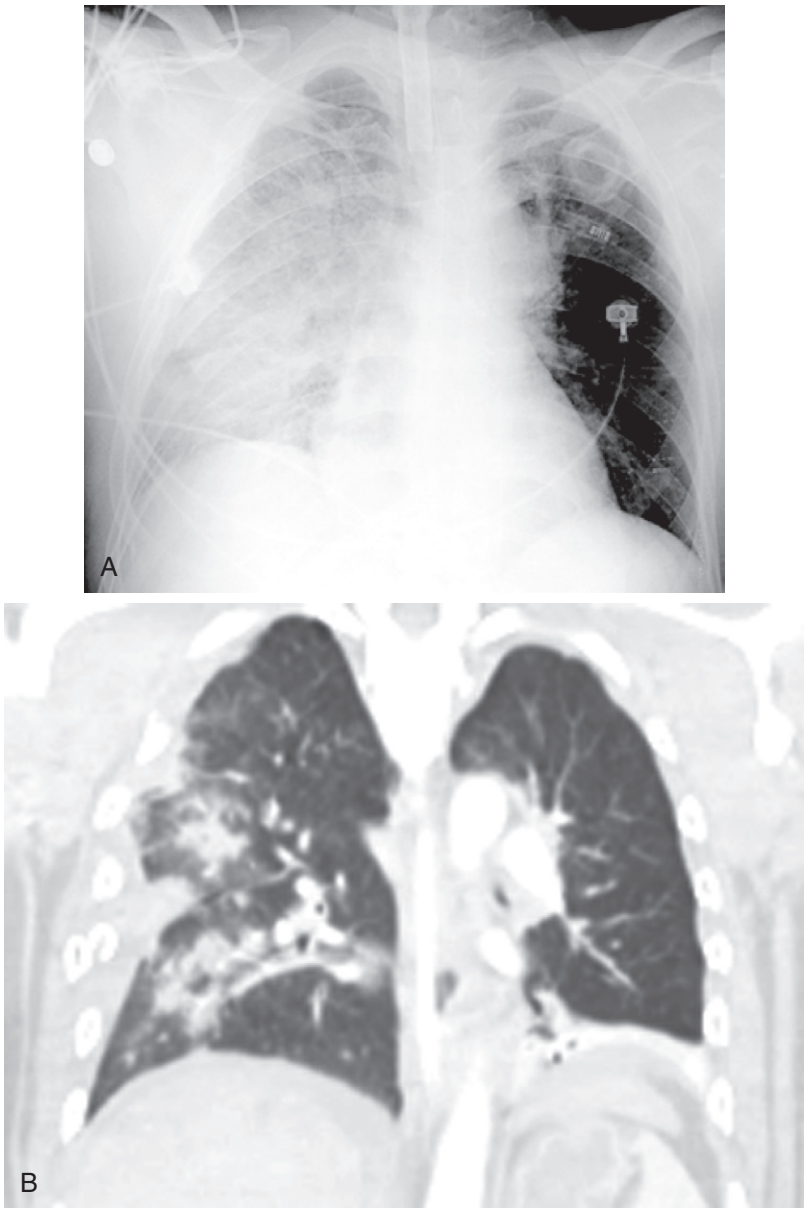

Figure 15-8 **A,** The confluent opacites of contusion are often not diffuse and uniform but more localized to the areas of most severe injury. This patient's injury is limited to the right lung. **B,** Coronal CT reveals the opacities to be less uniform and more multifocal than they appear on the plain film.

on clinical grounds. Patients with diffusely coalescent, bilateral pneumonias are usually profoundly ill with an elevated temperature, elevated white blood cell count, severe dyspnea, and productive sputum.

Bronchopneumonia

Bronchopneumonias are the most common infections producing diffuse coalescent opacities. Gram-negative organisms are particularly notorious for producing such fulminant pneumonias.[314] This pattern is frequently preceded by films showing multifocal ill-defined opacities like those described in Chapter 16. There is a tendency for

the patient to have some volume loss because of the bronchial inflammation. The loss of volume may cause one lobe to appear predominantly involved during the course of the illness. In some cases, the radiologic patterns of bronchopneumonia and pulmonary edema are similar (see the initial description of Diffuse Air-Space Disease on p. 224), although an asymmetric, patchy, or even unilateral presentation (see Fig 15-2) is more consistent with the diagnosis of bronchopneumonia. (Answer to question 2 is *a*.) It must be remembered that pulmonary edema may also produce a patchy or asymmetric distribution when there are underlying diseases such as emphysema or pulmonary embolism. Clinical and laboratory data may be useful in distinguishing bronchopneumonia from pulmonary edema. Bronchopneumonia should result in a febrile response with productive, purulent sputum and leukocytosis. Culture of sputum and blood usually confirms the diagnosis and identifies the organisms.[67]

Viral Pneumonias

Although viral pneumonias are best known for producing a diffuse interstitial pattern (usually a fine reticular or fine nodular pattern), fulminant cases may also lead to diffuse air-space consolidations. In these cases, there is extensive edema into the alveolar spaces. HRCT reports indicate that the pattern varies dependent upon the severity ranging from ground-glass opacities with areas of consolidation to near-complete alveolar consolidation. This was reported in detail with descriptions of severe acute respiratory syndrome (SARS).[97,423,552] Viral pneumonia may be especially severe in immunologically compromised patients,[439] in particular those with hematologic malignancies, acquired immune deficiency syndrome (AIDS), or organ transplants, and especially those who are receiving immunosuppressive therapy. Severe viral pneumonia with air-space consolidation is infrequently encountered in the otherwise normal patient.

ARDS is a well-documented complication of a number of viral and mycoplasma infections,[205] and it is a likely explanation for the pattern of diffuse air-space opacites in patients with viral pnemonia. Chicken pox pneumonia carries a very high risk for this complication, especially in pregnant patients. ARDS is also a concern with emerging infections including SARS.[60,545] This complication could also be the cause for a high mortality rate in an influenza pandemic.

Aspiration Pneumonia

Aspiration pneumonia is another cause of diffuse coalescent opacities that should be diagnosed by correlating the radiologic appearance with the clinical setting. Aspiration pneumonia may produce diffuse bilaterally coalescent opacities, although these tend to be more localized than in pulmonary edema. Because the aspirated material usually goes to the dependent portions of the lung, the distribution of the radiologic abnormality is directly related to the position of the patient at the time of aspiration. Material aspirated while the patient is in the upright position tends to go to the medial basal segments of the lung and to the right middle lobe, whereas in the supine-patient–aspirated material tends to collect in the superior segments of the lower lobes and the posterior segments of the upper lobes. Knowledge of the material aspirated and of the patient's position at aspiration usually confirms the diagnosis. In the clinical setting, the postoperative or comatose patient is more susceptible to aspiration. Patients who are alcoholic are especially prone to aspiration pneumonia.

Chronic aspiration, on the other hand, is more difficult to confirm and requires careful evaluation of the patient's history. For example, air-space consolidation in the right middle lobe in an elderly patient who is otherwise not particularly ill should prompt suspicion of an exogenous lipoid pneumonia (mineral oil aspiration). This type of aspiration pneumonia should not result in diffuse confluent opacities. Patients with disturbances of esophageal motility, obstructive lesions of the esophagus, and

head or neck tumors are all candidates for chronic aspiration. Aspiration may also be the underlying factor in the tendency for these patients to have gram-negative pneumonias. The gram-negative pneumonias are a much more likely cause of diffuse confluent opacities than is uncomplicated chronic aspiration.

Opportunistic Pneumonias

Immunologically compromised patients are susceptible not only to common pyogenic, viral, and fungal pneumonias, but also to a more virulent infection. Viral infections that may cause minimal abnormality in a patient with a competent immune system may cause a fatal hemorrhagic pneumonia in a patient with severe immune suppression. Fungi that are nonpathogenic in patients with normal immunity may cause diffuse coalescent opacities in the patient who is immunologically compromised.[548] These uncommon pathogenic fungi include *Aspergillus, Candida, Cryptococcus,* and *Phycomycetes*.[482] Infection by *Phycomycetes* is commonly called *mucormycosis*. Both *Phycomycetes* and *Aspergillus* invade the pulmonary vessels, leading to a diffuse hemorrhagic pneumonia and even pulmonary necrosis or gangrene.

AIDS-Related Diseases

Individuals infected with human immunodeficiency virus (HIV) are at risk for a variety of pulmonary infections, neoplasms, and drug reactions. *Pneumocystis carinii* pneumonia (PCP) is caused by a fungus that has been renamed *Pneumocystis jiroveci*. PCP is one of the most common infections in patients with AIDS,[259,758] occurring in more than 75% of patients. It is not expected to occur until the CD4 cell count has dropped to less than 200 cells/μl, but it is one of the most common AIDS-defining diseases.[299,707] The organisms spread through the airways and interstitium with minimal or no visible abnormality on the initial radiograph. During the earliest stages, gallium scans and HRCT are more sensitive for early diagnosis. The earliest plain film appearance is a subtle, fine, reticular pattern, but many cases follow a more fulminant course, with rapid development of diffuse coalescent opacities (Figs 15-9, *A-C*). This development results from alveolar wall injury followed by filling of the air-spaces with plasma proteins, inflammatory cells, and organisms. The plain film appearance is often that of diffuse symmetric coalescent opacities that resembles noncardiac edema (Fig 15-10). CT often confirms a mixed pattern of reticular interstitial opacities with thickening ot the interlobular septa, ground-glass opacites, and alveolar consolidation. The combination of interlobular septal thickening and ground-glass opacities is common and described as the "crazy-paving pattern."[297,627] An atypical, upper-lobe distribution may result in patients who are receiving prophylactic treatment with aerosolized pentamidine (Figs 15-11, *A* and *B*).[96,126] Associated pleural effusions are rare in patients with PCP, occurring as infrequently as in 2% of patients, and should be considered evidence of another diagnosis.

Pyogenic pneumonias are seen in 5% to 30% of HIV-infected people, but they typically occur in the earlier stages of infection, that is, before the first AIDS-defining disease. CD4 counts are usually between 200 and 500 cells/μl. Bacterial pneumonias may be severe and cause a pattern of diffuse consolidations in approximately 20% of cases, but lobar consolidations are more common with a frequency of 50%. The most common organisms are *Haemophilus influenzae* and *Streptococcus pneumoniae*.[139]

Kaposi's sarcoma and lymphoma are common neoplasms in patients with AIDS, but their plain film findings are most often either masses or multiple, poorly defined opacities rather than diffuse coalescent opacities (see Chapter 16). Lymphocytic interstitial pneumonia (LIP) is a lymphoproliferative disorder of the lung that is rare in patients with normal immunity but more common in patients with AIDS.[484] In patients without AIDS, LIP is a B-cell lymphocytic infiltration of the interstitium and alveolar walls; in patients with AIDS, it is a T-cell infiltration. AIDS-related LIP is rare in adults,

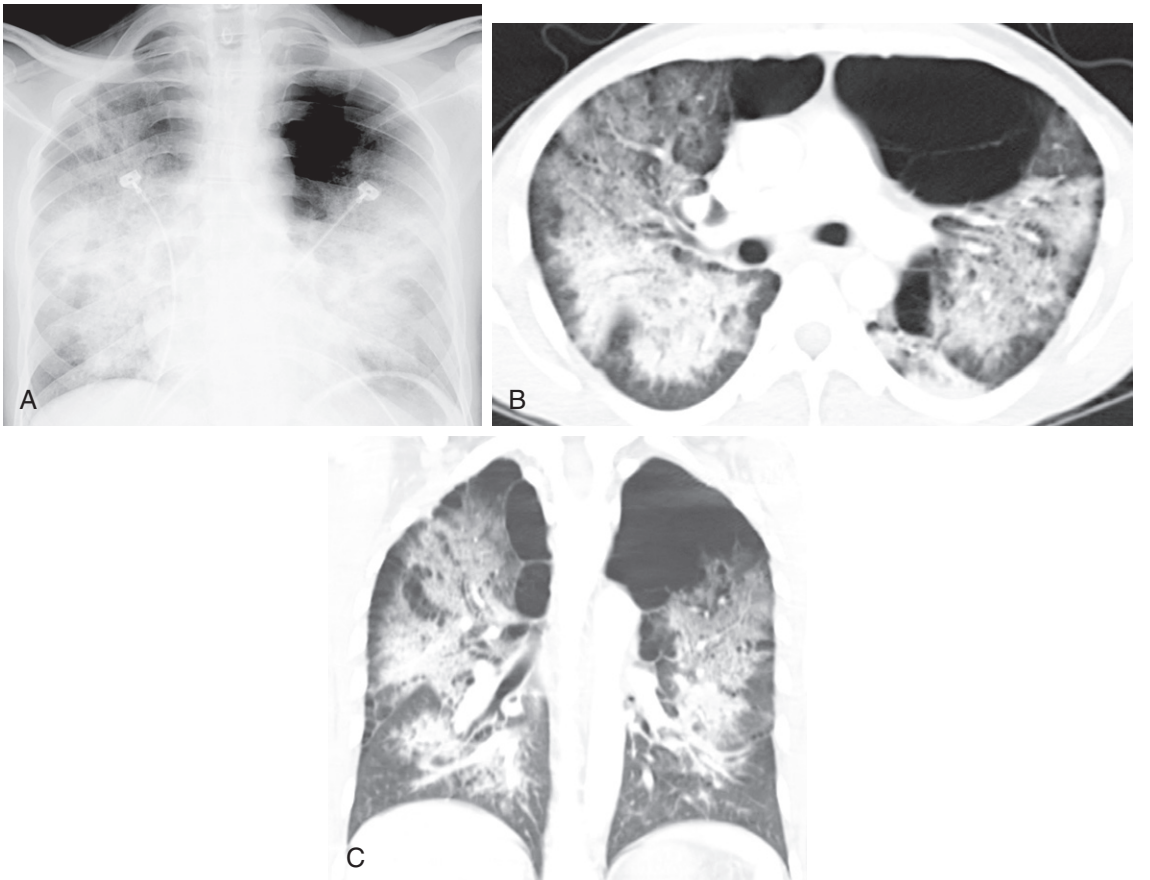

Figure 15-9 **A,** Diffuse bilateral confluent opacites in a patient with AIDS are strongly suggestive of PCP. **B,** Axial CT confirms the presence of extensive, bilateral alveolar consolidations and ground-glass opacities. The upper lobes are spared because of severe bullous disease. **C,** Coronal CT shows the opacities to have air bronchograms and a distribution resembling pulmonary edema.

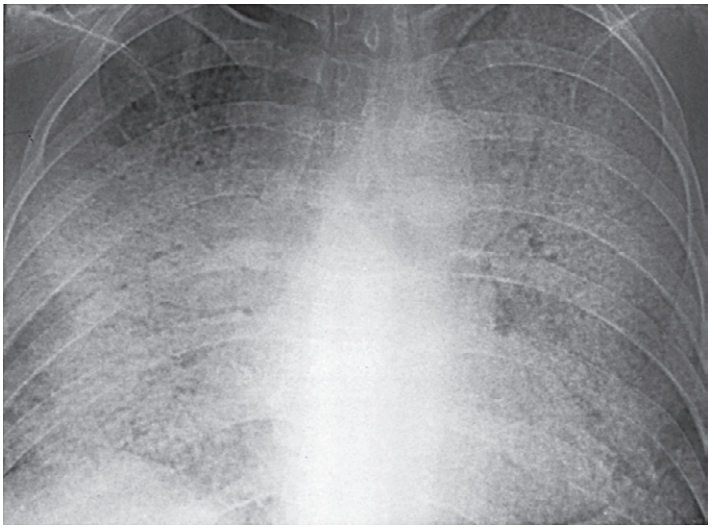

Figure 15-10 Pneumocystis pneumonia often causes a pattern of diffuse symmetric air-space opacities with air bronchograms. This may be confused with noncardiac pulmonary edema.

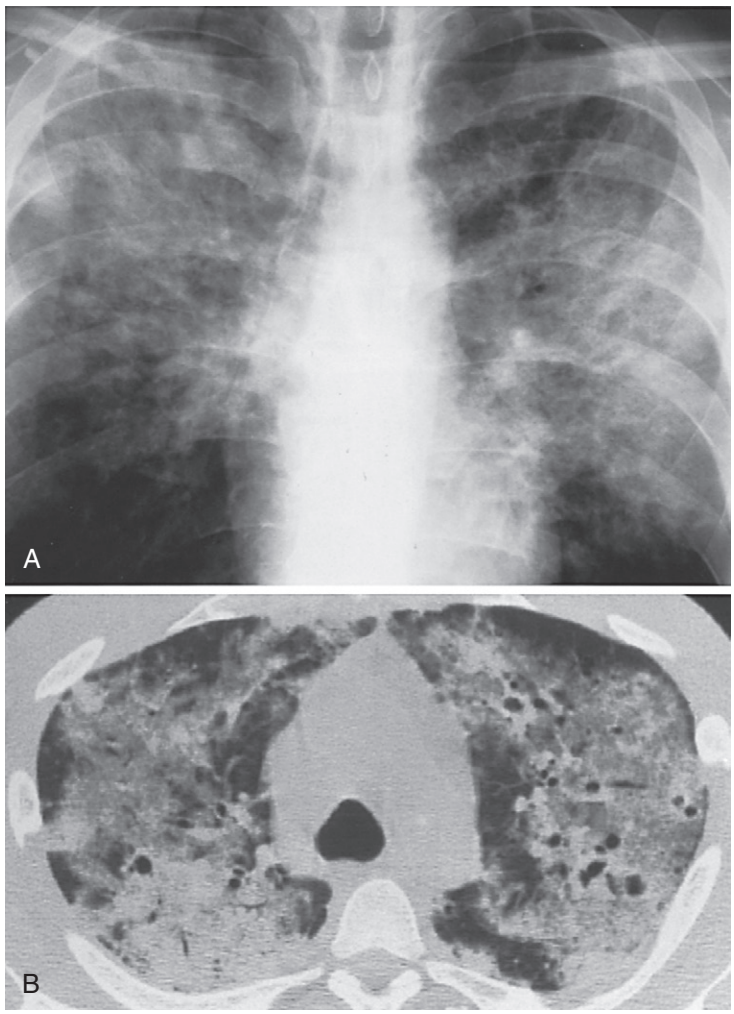

Figure 15-11 **A,** Prophylactic treatment of patients with AIDS for PCP may cause an atypical, upper-lobe distribution of the infection. In this case, there are confluent opacities in both upper lobes with sparing of the bases. **B,** A high-resolution CT section at the level of carina shows some consolidation of the posterior segment of the right upper lobes, but extensive ground-glass opacity in both upper lobes. Also note the scattered cystic lesions (see Chapter 24), which are a common complication of PCP in patients with AIDS.

but it is the second most common disease seen in children with AIDS, occuring in 30% of cases.

CHRONIC DIFFUSE CONSOLIDATIONS

Diffuse coalescent opacities usually indicate either an acute process, such as pulmonary edema, or the acute phase of a chronic relapsing disease, such as idiopathic pulmonary hemosiderosis. However, although rare, there are a few conditions that cause persistent chronic diffuse pulmonary consolidations. This somewhat rare radiologic presentation may be seen with chronic granulomatous diseases, neoplasms, and pulmonary alveolar proteinosis.

Chronic Granulomatous Diseases

Chronic granulomatous diseases rarely cause diffuse coalescent opacities. Fungal infections may produce this pattern in immunologically compromised patients but rarely

in the uncompromised host. Although rarely seen in tuberculosis, this pattern may occur when there is extensive pulmonary hemorrhage in conjunction with aspiration of blood to other portions of the lung from a cavitary lesion or when patients with miliary tuberculosis develop secondary pulmonary edema or ARDS.[527] Once this complication develops, the underlying miliary nodules are obscured by pulmonary edema.

Sarcoidosis is a rare cause of diffuse bilaterally symmetric consolidations that may resemble pulmonary edema. The mechanism for this pattern is considered in detail in Chapter 16. Sarcoidosis more often causes multifocal ill-defined opacities, which may have air bronchograms, than a pattern of diffuse confluent opacities. In contrast to all the other entities considered in this chapter, there may be a striking disparity between the severity of the radiologic appearance of sarcoidosis and the clinical well-being of the patient. Although the abnormalities may appear to be very extensive, patients with sarcoidosis are often only mildly dyspneic and may otherwise be asymptomatic.

Neoplasms

Diffuse coalescent opacities are rarely caused by neoplastic processes, but two categories of tumors do result in this pattern: (1) bronchiolalveolar cell carcinoma and (2) lymphoid disorders.

Bronchioloalveolar cell carcinoma is a unique airway neoplasm that arises in either the distal small bronchioles or alveolar walls. In its localized form, bronchioloalveolar cell carcinoma often produces an appearance more suggestive of a consolidation than a mass. Air bronchograms through the area of tumor are a common and distinctive feature of this tumor not often encountered in any other type of primary lung tumor. The air bronchograms may be enhanced by CT.[8] Bronchioloalveolar cell carcinoma frequently grows along alveolar walls and produces mucus within the air spaces. The alveolar walls and bronchi remain intact. Examination of histologic sections frequently reveals plugs of tumor in the bronchi, which supports the theory of bronchogenic spread of bronchioloalveolar cell carcinoma. This theory is consistent with the observation that the carcinoma may lead to multifocal, ill-defined opacities followed by diffuse air-space consolidations. In those cases with advanced pulmonary spread, HRCT shows a combination of air-space consolidation and ground-glass opacities.[729] The same mechanism of spread may also account for the occasional lobar consolidations that mimic lobar pneumonia. Because of the large amount of mucus and tumor tissue in the air spaces, cytologic examination often provides the diagnosis. Since the radiologic appearance of bronchioloalveolar cell carcinoma (Fig 15-12) is remarkably similar to that of pneumonia, the presence of a chronic, more persistent air-space consolidation frequently requires biopsy for definitive diagnosis.

Lymphoid disorders are another major category of neoplastic disease that may lead to diffuse air-space consolidation (see Chart 15-1). Like bronchioloalveolar cell carcinoma, lymphoma of the lung tends to be a localized process. Multifocal areas of air-space consolidation, as discussed in Chapter 16, are much more common than diffuse air-space consolidation, but the latter does occur. In the case of lymphocytic interstitial pneumonia, serial films may reveal an evolution of opacities from a diffuse reticular pattern to a confluent pattern. This once rare disease is now seen with increasing frequency in AIDS patients.[542]

Alveolar Proteinosis

Alveolar proteinosis[226,623] is an unusual disease that results in diffuse bilateral confluent opacities that often have air bronchograms (Figs 15-13, *A-D*). Occasionally, a fine, nodular pattern with ill-defined borders may be seen around the periphery of the confluent opacities, but these are not interstitial nodules like the nodules discussed in

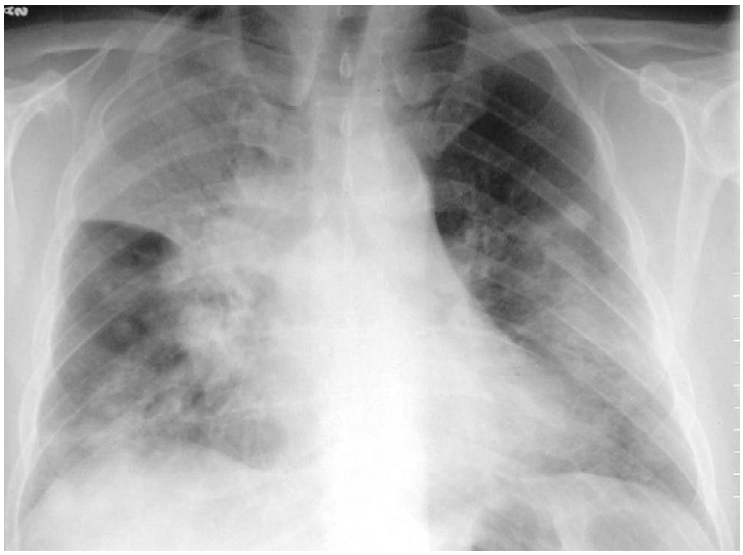

Figure 15-12 Bronchioloalveolar cell carcinoma often produces confluent air-space opacities that resemble pneumonia. This patient has consolidation of the right upper lobe with multiple opacities in the right-lower lung and scattered opacities throughout the left lung. The distribution of the opacities makes pulmonary edema unlikely, but other causes of air-space opacities, especially pneumonia or hemorrhage, could produce this appearance.

Chapter 17. They apparently represent the smallest unit of air-space filling that can be recognized radiologically. Ziskind referred to these fine opacities as *acinar rosettes*.[826] CT usually confirms extensive air-space consolidation, but also reveals ground-glass opacites, and thickened interlobular septa,[337]or the crazy-paving pattern.[627] This is a pathologic accumulation of surfactant in the alveoli. These consolidations may appear acutely and resolve spontaneously or may persist, requiring pulmonary lavage. The time required for their spontaneous resolution is highly variable. Alveolar proteinosis is also observed to be a chronic relapsing disease and one of the few diseases that may produce diffuse air-space consolidation while the patient remains relatively asymptomatic. In fact, the radiologic presentation of diffuse bilateral air-space consolidations that are either recurrent or chronic in a patient who complains only of mild dyspnea strongly suggests this diagnosis.

Top 5 Diagnoses: Diffuse Air-Space Opacities

1. Edema
2. Bronchopneumonia
3. ARDS
4. PCP
5. Hemorrhage

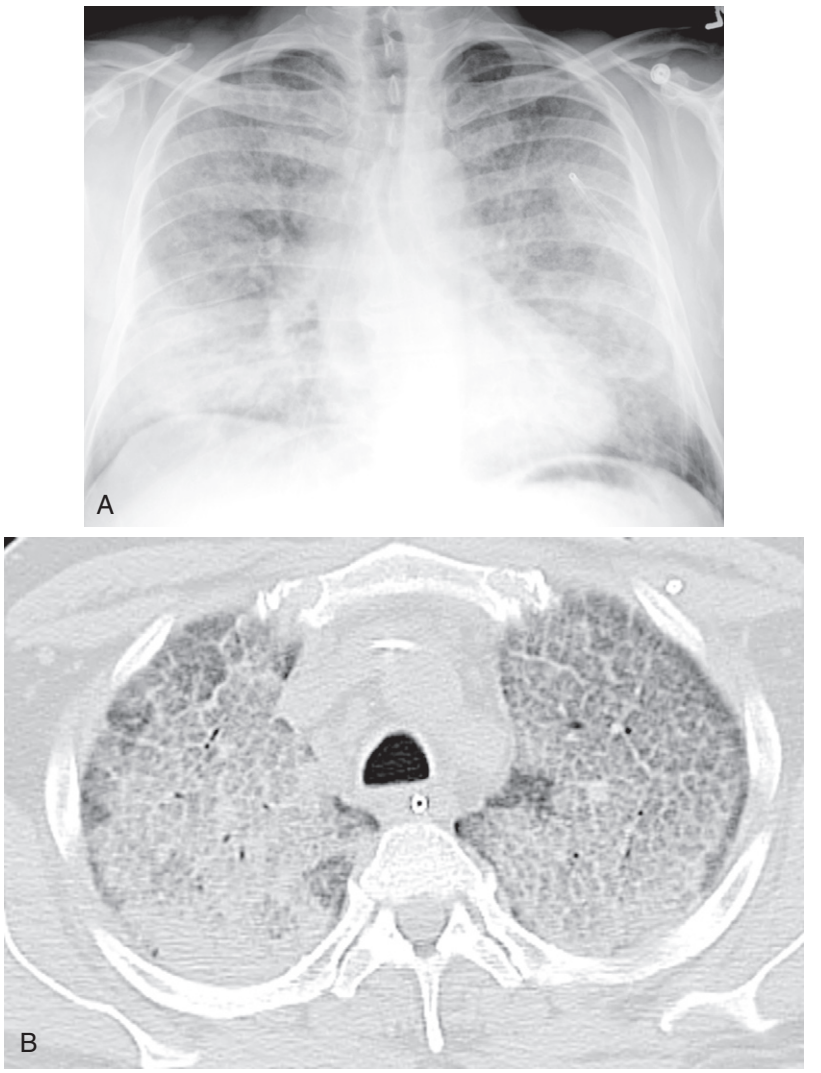

Figure 15-13 **A,** Diffuse bibasilar confluent opacities fade into the more normal-appearing, aerated lung with an intermediate, poorly defined, ground-glass appearance. This radiologic appearance is similar to pulmonary edema, hemorrhage, and diffuse pneumonia, but this patient's opacities were chronic and relapsing. **B,** Axial CT through the upper lungs confirms extensive ground-glass opacities with associated thickening of the interlobular septa. This combination is described as the "crazy-paving pattern."

Summary

Diffuse coalescent opacities with air bronchograms, air alveolograms, and acinar rosettes constitute the classic radiologic appearance of alveolar disease. Pure alveolar disease is rarely seen, alveolar proteinosis being one of the very few examples. The other entities listed in Chart 15-1 are all examples of mixed alveolar and interstitial disease.

The underlying, interstitial component of the disease is obscured by the alveolar disease.

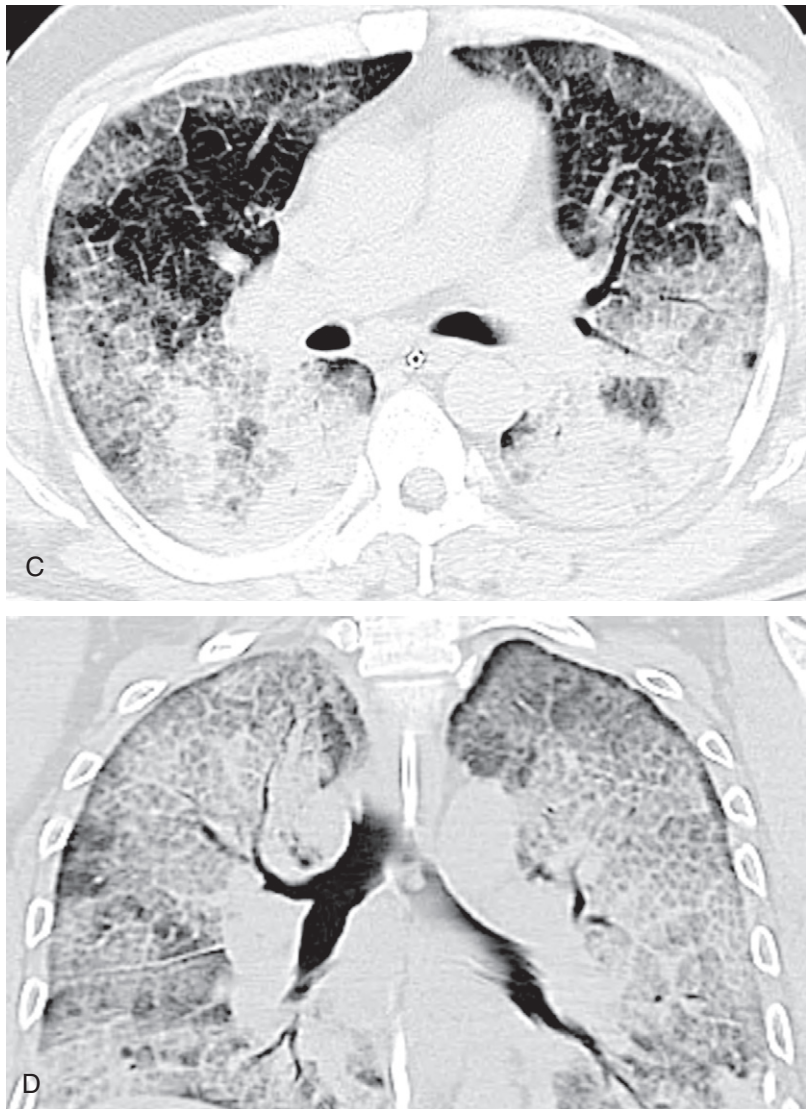

Figure 15-13, cont'd C, At the level of the carina, there is a mixed pattern with air-space consolidations, air bronchograms, ground-glass opacities, and normally aerated lung. **D,** Coronal reconstructions demonstrate the diffuse distribution of the air space and ground-glass opacites in this patient with pulmonary alveolar proteinosis. These plain film and CT patterns in combination with the history of a chronic and relapsing clinical course are the expected presentation of pulmonary alveolar proteinosis.

The most common cause of this pattern is pulmonary edema. Pulmonary edema may be divided into cardiac and noncardiac categories on the basis of cause. Clinical correlation is extremely important in identifying the cause in pulmonary edema of noncardiac origin.

ARDS is a complex clinical syndrome that results in diffuse coalescing opacities. The diagnosis should be suspected when the patient has acute pulmonary edema following severe injury or shock, particularly after drug reactions, gram-negative sepsis, transfusion reactions, snake bite, or the use of pump oxygenators in cardiopulmonary bypass surgery.

Diffuse pneumonias are another extremely important cause of diffuse coalescent opacities. They should be easily distinguished from pulmonary edema when seen in an acutely ill and toxic, febrile patient. The causal agents are frequently gram-negative organisms. The radiologic appearance is of little value in determining the specific organism. Viruses and fungi may also produce this pattern, particularly in the immunologically compromised host. Prompt diagnostic biopsy is essential in the compromised host, because failure to initiate immediate therapy may result in death.

Diffuse pulmonary hemorrhage with extensive bilateral confluent opacities is frequently but not invariably associated with hemoptysis. Clinical correlation is essential in determining the cause of diffuse pulmonary hemorrhage (anticoagulation therapy, hemophilia, leukemia, or trauma). Biopsy is required for a diagnosis of the idiopathic sources of such hemorrhage, including Goodpasture's syndrome, pulmonary hemosiderosis, and Wegener's granulomatosis.

Bronchioloalveolar cell carcinoma and lymphoid disorders of the lung are the only neoplastic conditions likely to result in this pattern.

ANSWER GUIDE

Legends for introductory figures

Figure 15-1 **A,** Pulmonary hemorrhage fills the alveoli with blood and often causes bilateral symmetric, coalescent opacities. This patient presented with massive hemoptysis. The bleeding was the result of pulmonary vasculitis from Wegener's granulomatosis. **B,** Coronal reconstruction emphasizes the diffuse alveolar consolidation with air bronchograms.

Figure 15-2 Bronchopneumonia has caused consolidation of the entire right lung. Note the air-filled branching bronchial tree. Air bronchograms are a reliable sign of pulmonary consolidation.

ANSWERS

1. a, b, c, e 2. a 3. c